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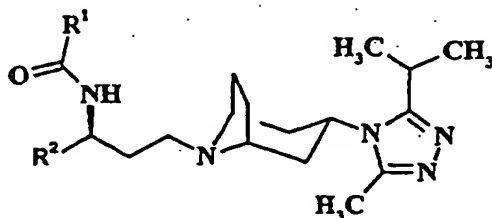
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(54) Title: TROPANE DERIVATIVES USEFUL IN THERAPY



(I)

(57) Abstract: The present invention provides compounds of the formula (I): wherein R¹ is C₃₋₆ cycloalkyl optionally substituted by one or more fluorine atoms, or C₁₋₆ alkyl optionally substituted by one or more fluorine atoms, or C₃₋₆ cycloalkylmethyl optionally ring-substituted by one or more fluorine atoms; and R² is phenyl optionally substituted by one or more fluorine atoms, to pharmaceutically acceptable salts and solvates thereof, and to processes for the preparation of, intermediates used in the preparation

of, compositions containing and the uses of, such compounds.

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Tropane derivatives useful in therapy

This invention relates to tropane derivatives useful in the treatment of a variety of disorders, including those in which the modulation of CCR5
5 receptors is implicated. More particularly, the present invention relates to 3-(3-isopropyl-5-methyl-4H-1,2,4-triazol-4-yl)-exo-8-azabicyclo[3.2.1]octane derivatives and to processes for the preparation of, intermediates used in the preparation of, compositions containing and the uses of, such derivatives. Disorders that may be treated or prevented by the present derivatives include
10 HIV and genetically related retroviral infections (and the resulting acquired immune deficiency syndrome, AIDS), and inflammatory diseases.

The compounds of the present invention are modulators, especially antagonists, of the activity of chemokine CCR5 receptors. Modulators of the CCR5 receptor may be useful in the treatment of various inflammatory
15 diseases and conditions, and in the treatment of infection by HIV-1 and genetically related retroviruses. The name "chemokine", is a contraction of "chemotactic cytokines". The chemokines comprise a large family of proteins which have in common important structural features and which have the ability to attract leukocytes. As leukocyte chemotactic factors, chemokines
20 play an indispensable role in the attraction of leukocytes to various tissues of the body, a process which is essential for both inflammation and the body's response to infection. Because chemokines and their receptors are central to the pathophysiology of inflammatory and infectious diseases, agents which are active in modulating, preferably antagonizing, the activity of chemokines
25 and their receptors, are useful in the therapeutic treatment of such inflammatory and infectious diseases.

The chemokine receptor CCR5 is of particular importance in the context of treating inflammatory and infectious diseases. CCR5 is a receptor for chemokines, especially for the macrophage inflammatory proteins (MIP)
30 designated MIP-1 α and MIP-1 β , and for a protein which is regulated upon activation and is normal T-cell expressed and secreted (RANTES).